

### REMARKS

Claims 16-18 and 21 are pending in the application. Claims 1-15, 19, and 20 have been cancelled without prejudice. Claim 16 has been amended. Claims 17, 18, and 21 are withdrawn from consideration as being drawn to non-elected species. The specification has been amended to divide the paragraph beginning at page 16, line 2 into three separate paragraphs. No new matter has been added.

#### Double Patenting

At pages 3-4 of the Office Action, claims 19 and 20 were rejected on the ground of nonstatutory obviousness-type double patenting over claim 1 of U.S. Patent No. 7,452,670 ("the '670 patent"). Claims 19 and 20 have been cancelled without prejudice, thereby rendering the present rejection moot.

At pages 4-5 of the Office Action, claim 16 was rejected on the ground of nonstatutory obviousness-type double patenting over claim 1 of the '670 patent in view of Duchen (2004) Diabetes 53:S96-S102.

Applicants respectfully traverse the rejection in view of the following remarks.

As detailed in the working examples section of the specification, the inventors of the present application discovered that ruthenium red (a mitochondrial  $\text{Ca}^{++}$  porter) suppresses alpha synuclein-mediated toxicity in yeast expressing two copies of alpha synuclein (see Example 2 at page 32, lines 4-12 of the specification). Consistent with this experimental finding, claim 16 is directed to a method of identifying a compound that inhibits alpha synuclein-mediated toxicity by: providing a yeast cell expressing an amount of alpha synuclein that reduces viability of the cell; contacting the cell with a candidate agent selected from several agents including a mitochondrial  $\text{Ca}^{++}$  porter (the elected species); and determining whether the candidate agent enhances viability of the cell.

The '670 patent does not suggest using ruthenium red as a means to suppress alpha synuclein-mediated toxicity. Duchen does not add what is lacking in the '670 patent. With

respect to alpha synuclein and Parkinson's disease, Duchen contains only a general statement that mitochondrial dysfunction has been implicated in Parkinson's disease (S97, left column). In a separate section of the publication reviewing mitochondrial bioenergetics and cellular calcium signaling, Duchen states that ruthenium red blocks the activity of an electrogenic uniporter that carries calcium into the mitochondria and that calcium that is accumulated by mitochondria must be removed (S97, right column). However, nothing in Duchen would have led the person of ordinary skill in the art to reasonably expect that mitochondrial calcium would be relevant to Parkinson's disease and that ruthenium red would be effective at suppressing alpha synuclein-mediated toxicity. Duchen's general statement that ruthenium red blocks the activity of a uniporter that carries calcium into the mitochondria would not have led to such an expectation. In the absence of a basis to reasonably expect that ruthenium red would suppress alpha synuclein-mediated toxicity, the person of ordinary skill in the art would have had no rationale for using ruthenium red in the practice of the claimed method. As a result, the combination of the '670 patent and Duchen does not render claim 16 unpatentable.

35 U.S.C. § 102(e)

At pages 6-7 of the Office Action, claims 19 and 20 were rejected under 35 U.S.C. § 102(e) as being anticipated the '670 patent". Claims 19 and 20 have been cancelled without prejudice, thereby rendering the present rejection moot.

35 U.S.C. § 103(a)

At pages 7-9 of the Office Action, claim 16 was rejected under 35 U.S.C. § 103(a) as being unpatentable over the '670 patent in view of Duchen for the same reasons provided in the double patenting rejection above. Applicants respectfully submit that the '670 patent and Duchen do not render claim 16 obvious for the same reasons provided above in the response to the double patenting rejection.

### Claim Objection

At page 11 of the Office Action, the Examiner objected to claim 16, asserting that the claim is not in proper grammatical form. Claim 16 has been amended in the manner suggested in the Office Action.

### Objection to Disclosure

At page 11 of the Office Action, the Examiner objected to the lack of spacing between sentences in the first full paragraph on page 16. The specification has been amended to address the spacing issue by providing three separate paragraphs.

### CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Enclosed is a Petition for Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply other any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 17481-0002US1.

Respectfully submitted,

Date: August 17, 2011

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